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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/423,126	11/05/1999	AKSEL BUCHTER-LARSEN	674509-2020	6366

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EXAMINER

KALLIS, RUSSELL

ART UNIT PAPER NUMBER

1638

DATE MAILED: 05/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/423,126

Applicant(s)

BUCHTER-LARSEN ET AL.

Examiner

Kallis

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 February 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,9,21 and 26-39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,9,21 and 26-39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: *Beta & Sons*

DETAILED ACTION

Specification

1. All previous rejections have been withdrawn in view of the following new groups of rejections. Therefore, Applicant's arguments filed 2/8/02 are deemed moot.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Process for preparing an anti-oxidant in a plant by transformation with a glucan lyase DNA.

Claim Objections

2. Claims 9 and 29-39 are objected to because of the following informalities: The claims are drawn to non-elected subject matter (SEQ ID NO: 8-12). Applicant must amend claims to delete non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 21, 26-31, 33-35, and 37-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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Applicant claims a method of plant transformation with a glucan lyase DNA. Applicant describes a single genomic sequence from a red algae that encodes glucan lyase (SEQ ID NO: 7). Applicant does not describe other DNA sequences that encode glucan lyase, especially those that have 75%, 85%, or 90% sequence homology to the sequence set forth in SEQ ID NO: 7. Therefore it is unclear from the instant specification that Applicant was in possession of the invention as broadly claimed.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

5. Claims 1, 21, 26-31, 33-35, and 37-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant claims a method for addition of an antioxidant to foodstuffs and for improving the transformation of a plant by transforming and expressing in a plant a glucan lyase gene, or a variant of a glucan lyase gene having 75%, 85%, and 90% nucleotide sequence identity to SEQ ID NO: 7, that produces an antioxidant, anhydrofructose.

Applicant teaches by reference (WO95/10618, page 12 line 14), the isolation of a nucleotide sequence (SEQ ID NO: 7) that encodes a glucan lyase from a fungus that infects algae

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and expresses α -1,4-glucan lyase. Applicant also provides guidance for various methods of plant transformation on pages 16-31.

Applicant does not teach DNA sequences or the isolation of DNA sequences from a broad category of glucan lyases or glucan lyases with 75%, 85%, and 90% sequence identity to any nucleotide sequence that encodes a glucan lyase. Applicant does not teach how to make homologues of a glucan lyase or effectively screen the myriad of possible DNA sequences or analyze for functionally complete gene products.

The unpredictability of predicting enzyme activity based upon sequence identities that vary between 10% to 25% can be extrapolated from the example where a small number of changes have been introduced into proteins that are well characterized with regard to their structure, and the results revealed that the structural determinants were more complex than believed (Guinto, E R. *et al.* PNAS, USA Vol. 96, pp. 1852-1857, March 1999; Unexpected crucial role of residue 225 in serine proteases, and Preiss, J. *et al.* Biochem and Biophysical Research Communications, 244, pp. 573-577, 1998; Functional Analysis of Conserved Histidines in DAP-Glucose Pyrophosphorylase from *Escherichia coli*). The unpredictability in the art is due to the absence of predictive rules for protein folding (Alberghina, L. ed., chapter 1 p. 9, in Protein Engineering in Industrial Biotechnology, ISBN 90-5702-412-8, Harwood Academic Publishers 2000) and the lack of knowledge about the structure of glucan lyase. Hence, one cannot readily predict enzyme activity based upon discreet changes or changes in amino acid composition resulting from gross divergence from sequence identity.

In the case of determining which amino acid residues, or combination of residues, when changed would be permissive of an embodiment of the invention, a person of average skill in the

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art would have to either test them experimentally for activity *in vitro* and *in planta*, or resort to *de novo* methods to find a sequence that would convert α -1,4-glucan to 1,5-D-anhydrofructose by α -1,4-glucan lyase. Therefore, undue trial and error experimentation would be required to screen through the multitude of nucleic acids encoding proteins with any of the myriad of different amino acid substitutions to identity those that convert α -1,4-glucan to 1,5-D-anhydrofructose, and hence could be used in the claimed invention.

The substrate specificity of α -1,4-glucan lyase is for α -1,4-glucan as stated in the abstract by Yu *et al.* in Biochim Biophys Acta 1993 Mar 21;1156. Clearly the recombinant enzyme in the claims is α -1,4-glucan lyase. The specification does not provide guidance for the conversion of any glucan, for example a 1,6-glucan, to 1,5-D-anhydrofructose by α -1,4-glucan lyase.

Furthermore, Applicant has claimed a method of producing anhydrofructose whereas Applicant has only taught production of 1,5-D-anhydrofructose. The unpredictability and the lack of guidance provided for engineering α -1,4-glucan lyase to convert any glucan into any anhydrofructose would require an undue amount of experimentation for one of skill in the art.

Given the lack of guidance, the absence of working examples in the specification that reflect the breadth of the claims, and the unpredictability in the art, undue trial and error would be needed to practice the invention. Therefore, the invention is not enabled.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 21, 28-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 21 recites the limitation "improving the transformation" in line 1. It is not clear how the transformation is to be improved.

Claims 29-39 recite the term "homology", which is an archaic term in the art and considered indefinite because it is not known whether it means evolutionary relatedness. It should be changed to --identity--.

Claim 36 recites the limitation "wherein the recombinant enzyme" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 37-38 recite the limitation "wherein the enzyme" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 21, 28, and 32-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu *et al.* (U.S. Patent 6,013,504) in view of Perl *et al.* (Nature Biotechnology, Vol. 14 May, 1996).

Applicant claims a process for the improving the transformation of grape by means of expressing a recombinant enzyme in a plant or part thereof. The recombinant enzyme, a glucan lyase, encoded by SEQ ID NO: 7, acts on a glucan substrate to produce an antioxidant, anhydrofructose.

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Yu *et al.* disclose a DNA sequence encoding a fungal glucan lyase, having 100% homology to the glucan lyase encoded by SEQ ID NO: 7 of the instant application, and a method for the *in situ* production, thereby, of 1,5-anhydrofructose in cellular organisms that lack this starch/glycogen degradation pathway catalyzed by α -1,4-glucan lyase, in column 16 lines 25-29 and 36-56.

Yu *et al.* do not disclose a method of grape transformation using antioxidants to improve the transformation process.

Perl *et al.* discloses a method of transformation of grape whereby inhibition of necrosis in grape tissue by the addition of antioxidants resulted in improved transformation (Abstract).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the invention of Yu *et al.* for production of anhydrofructose by expressing the α -1,4-glucan lyase in a host capable of the starch degradation pathway to transform grape as taught by Perl rather than a cellular organism. One having ordinary skill in the art would have been motivated by Perl *et al.* page 1, column 1 lines 1-4, to improve transformation of grape by addition of an antioxidant, anhydrofructose, thereby increasing the number of stable transformants.

Claims 1, 9, 26-27 and 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu *et al.* (U.S. Patent 6,013,504) in view of Perl *et al.* (Nature Biotechnology, Vol. 14 May, 1996).

Applicant claims a process for the production of an antioxidant in grape by means of expressing, in a plant or part thereof, glucan lyase, a recombinant enzyme encoded by SEQ ID

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NO: 7, that acts on a glucan substrate to produce anhydrofructose, an antioxidant comprised by the food product, made from the transformed grape, wine.

Yu *et al.* disclose a DNA sequence encoding a fungal glucan lyase, having 100% homology to the glucan lyase encoded by SEQ ID NO: 7 of the instant application, and a method for the *in situ* production, thereby, of 1,5-anhydrofructose in cellular organisms that lack this starch/glycogen degradation pathway catalyzed by α -1,4-glucan lyase, in column 16 lines 25-29 and 36-56.

Yu *et al.* do not disclose a method for the production in transformed grape, of an antioxidant, anhydrofructose, and wine made from the transformed grape that comprises the antioxidant, anhydrofructose.

Perl *et al.* discloses a method of transformation of grape, *vitis vinifera*, whereby inhibition of necrosis in grape tissue by the addition of antioxidants resulted in improved transformation (Abstract).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the invention of Yu *et al.*, of expressing α -1,4-glucan lyase in a host capable of the starch degradation pathway for *in planta* production of the antioxidant, anhydrofructose, in wine grapes as taught by Perl. It further would have been obvious to make wine from the transformed grape that would comprise the antioxidant, anhydrofructose. One of skill in the art would have been motivated by the successful transformation of the variety of grape used in wine making, *vitis vinifera*, by Perl *et al.* (page 1, column 1 lines 1-19).

10. All claims are rejected.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Kim Davis, whose telephone number is (703) 308-0009.

Russell Kallis Ph.D.
April 29, 2002

A handwritten signature in black ink, appearing to read "Amy Nelson", with a stylized flourish at the end.

AMY J. NELSON, PH.D
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